REMARKS

Applicants here elect to proceed with the Group II invention, represented by claims 33-41. Applicant has further amended claims 2-32 of the Group I invention, to make them applicable to the Group II invention (by putting them into method claim format). Therefore, claims 2-41 are currently pending.

The Examiner is invited to contact the undersigned attorneyat (512) 536-3055 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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Date: 10/26/01

CLAIM AMENDMENTS: RESPONSE TO RESTRICTION REQUIREMENT

~~1. A composition for imaging comprising:~~

~~a radionuclide label;~~

~~ethylenedicysteine; and~~

~~a tissue specific ligand conjugated to said ethylenedicysteine;~~

~~wherein said ethylenedicysteine forms an N_2S_2 chelate with said radionuclide label.~~

2. The method ~~composition~~ of claim 33~~1~~, wherein said tissue specific is ~~ligand may be~~ conjugated to said ethylenedicysteine on ~~one or~~ both acid arms of the ethylenedicysteine.

3. The method ~~composition~~ of claim 33~~1~~, wherein said radionuclide is ^{99m}Tc, ^{188}Re, ^{186}Re, ^{183}Sm, ^{166}Ho, ^{90}Y, ^{89}Sr, ^{67}Ga, ^{68}Ga, ^{111}In, ^{183}Gd, ^{59}Fe, ^{225}Ac, ^{212}Bi, ^{211}At, ^{64}Cu or ^{62}Cu.

4. The method ~~composition~~ of claim 3, wherein said radionuclide is ^{99m}Tc.

5. The method ~~composition~~ of claim 35~~1~~, wherein said tissue specific ligand is an anticancer agent, DNA topoisomerase inhibitor, antimetabolite, tumor marker, folate receptor targeting ligand, tumor apoptotic cell targeting ligand, tumor hypoxia targeting ligand, DNA intercalator, receptor marker, peptide, nucleotide, organ specific ligand, antibiotic, antifungal, antibody, glutamate pentapeptide or an agent that mimics glucose.

6. The method ~~composition~~ of claim 5, wherein said tissue specific ligand is an anticancer agent.

7. The method ~~composition~~ of claim 6, wherein said anticancer agent may be selected from the group consisting of methotrexate, doxorubicin, tamoxifen, paclitaxel, topotecan, LHRH, mitomycin C, etoposide tomudex, podophyllotoxin, mitoxantrone, camptothecin, colchicine, endostatin, fludarabin, gemcitabine and tomudex.

8. The method ~~composition~~ of claim 5, wherein said tissue specific ligand is a tumor marker.

9. The method ~~composition~~ of claim 8, wherein said tumor marker is PSA, ER, PR, CA-125, CA-199, CEA AFP, interferons, BRCA1, HER-2/neu, cytoxan, p53, endostatin or a monoclonal antibody (e.g., antisense).

10. The method ~~composition~~ of claim 5, wherein the tissue specific ligand is a folate receptor targeting ligand.

11. The method ~~composition~~ of claim 10, wherein the folate receptor targeting ligand is folate, methotrexate or tomudex.

12. The method ~~composition~~ of claim 11, wherein the ligand derivative is ~~further defined as~~ ^{99m}Tc-EC-folate.

13. The method ~~composition~~ of claim 11, wherein the ligand derivative is ~~further defined as~~ ^{99m}Tc-EC-methotrexate.

14. The method ~~composition~~ of claim 11, wherein the ligand derivative is ~~further defined as~~ ^{99m}Tc-EC-tomudex.

15. The method ~~composition~~ of claim 5, wherein the tissue specific ligand is a tumor apoptotic cell targeting ligand or a tumor hypoxia targeting ligand.

16. The method ~~composition~~ of claim 15, wherein the tissue specific ligand is annexin V, colchicine, nitroimidazole, mitomycin or metronidazole.

17. The method ~~composition~~ of claim 16, wherein the ligand derivative is ~~further defined as~~ ^{99m}Tc-EC-annexin V.

18. The method ~~composition~~ of claim 16, wherein the ligand derivative is ~~further defined as~~ ^{99m}Tc-EC-colchicine.

19. The method ~~composition~~ of claim 16, wherein the ligand derivative is ~~further defined as~~ ^{99m}Tc-EC-nitroimidazole.

20. The method ~~composition~~ of claim 16, wherein the ligand derivative is ~~further defined as~~ ^{99m}TC-EC-metronidas.

21. The method ~~composition~~ of claim 5, wherein the tissue specific ligand is glutamate pentapeptide ~~(molecular weight 750-15,000)~~.

22. The method ~~composition~~ of claim 0, wherein the ligand derivative is ~~further defined as~~ 99mTc-EC-glutamate pentapeptide.

23. The method ~~composition~~ of claim 5, wherein the tissue specific ligand is an agent that mimics glucose.

24. The method ~~composition~~ of claim 23, wherein the agent that mimics glucose is neomycin, kanamycin, getnamycin, paromycin, amikacin, tobramycin, netilmicin, ribostamycin, sisomicin, micromicin, lividomycin, dibekacin, isepamicin, astromicin, or an aminoglycoside.

25. The method ~~composition~~ of claim 24, wherein the ligand derivative is ~~further defined as~~ 99mTc-EC-neomycin.

26. The method ~~composition~~ of claim 24, wherein the ligand derivative is ~~further defined as~~ 99mTc-EC-kanamycin.

27. The method ~~composition~~ of claim 24, wherein the ligand derivative is ~~further defined as~~ 99mTc-EC-aminoglycosides.

28. The method ~~composition~~ of claim 24, wherein the ligand derivative is ~~further defined as~~ 99mTc-EC-gentamycin.

29. The method ~~composition~~ of claim 24, wherein the ligand derivative is ~~further defined as~~ 99mTc-EC-tobramycin.

30. The method ~~composition~~ of claim 2, further comprising a linker conjugating EC to said tissue specific ligand.

31. The method ~~composition~~ of claim 30, wherein the linker is a water soluble peptide, glutamic acid, aspartic acid, bromo ethylacetate, ethylene diamine or lysine.

32. The method ~~composition~~ of claim 31, wherein the tissue specific ligand is estradiol, topotecan, paclitaxel, raloxifen, etoposide, doxorubricin, mitomycin C, endostatin, annexin V, LHRH, octreotide, VIP, methotrexate or folic acid.

33. A method of synthesizing a radiolabeled ethylenedicysteine derivative for imaging comprising the steps:

a) obtaining a tissue specific ligand;

b) admixing said ligand with ethylenedicysteine (EC) to obtain an EC-tissue specific ligand derivative; and

c) admixing said EC-tissue specific ligand derivative with a radionuclide and a reducing agent to obtain a radionuclide labeled EC-tissue specific ligand derivative, wherein the EC forms an N_2S_2 chelate with the radionuclide.

34. The method of claim 33, wherein said reducing agent is a dithionite ion, a stannous ion or a ferrous ion.

35. A method for labeling a tissue specific ligand for imaging, comprising the steps:

a) obtaining a tissue specific ligand;

b) admixing the tissue specific ligand with ethylenedicysteine (EC) to obtain an EC-ligand drug conjugate; and

c) reacting the drug conjugate with ^{99m}Tc in the presence of a reducing agent to form an N_2S_2 chelate between the ethylenedicysteine (with or without linker) and the ^{99m}Tc.

36. The method of claim 35, wherein the tissue specific ligand is an anticancer agent, DNA topoisomerase inhibitor, antimetabolite, tumor marker, folate receptor targeting ligand, tumor apoptotic cell targeting ligand, tumor hypoxia targeting ligand, DNA intercalator, receptor marker, peptide, organ specific ligand, antibiotic, antifungal, glutamate pentapeptide or an agent that mimics glucose.

37. The method of claim 36, wherein the reducing agent is a dithionite ion, a stannous ion or a ferrous ion.

38. A method of imaging a site within a mammalian body comprising the steps of administering an effective diagnostic amount of a composition comprising a 99mTc labeled ethylenedicysteine-tissue specific ligand conjugate and detecting a radioactive signal from the ^{99m}Tc localized at the site.

39. The method of claim 38, wherein the site is a tumor.

40. The method of claim 38, wherein the site is an infection.

41. The method of claim 38, wherein the site is breast cancer, ovarian cancer, prostate cancer, endometrium, heart, lung, brain, liver, folate (+) cancer, ER (+) cancer, spleen, pancreas, or intestine.

~~42. A kit for preparing a radiopharmaceutical preparation, said kit comprising a sealed container including a predetermined quantity of an ethylenedicysteine-tissue specific ligand~~

conjugate composition and a sufficient amount of reducing agent to label the conjugate with ^{99m}Tc.

43. The kit of claim 42, wherein the ethylenedicysteine-tissue specific ligand conjugate composition further comprises a linker between the ethylenedicysteine and the tissue specific ligand.

44. The kit of claim 42, wherein the tissue specific ligand is an anticancer agent, DNA topoisomerase inhibitor, antimetabolite, tumor marker, folate receptor targeting ligand, tumor apoptotic cell targeting ligand, tumor hypoxia targeting ligand, DNA intercalator, receptor marker, peptide, organ ligand, antibiotic, antifungal, glutamate pentapeptide or an agent that mimics glucose.

45. The kit of claim 43, wherein the tissue specific ligand is estradiol, topotecan, paclitaxel, raloxifen, etoposide, doxorubricin, mitomycin C, endostatin, annexin V, LHRH, octreotide, VIP, methotrexate or folic acid.

46. The kit of claim 45, wherein the linker is a water soluble peptide, glutamic acid, polyglutamic acid, aspartic acid, polyaspartic acid, bromoethylacetate, ethylenediamine or lysine.

47. A reagent for preparing a scintigraphic imaging agent comprising a tissue specific ligand covalently linked to a ^{99m}Tc binding moiety.

48. The reagent of claim 47, wherein the ^{99m}Tc binding moiety is ethylenedicysteine.

49. The reagent of claim 48, wherein the tissue specific ligand is an anticancer agent, DNA topoisomerase inhibitor, antimetabolite, tumor marker, folate receptor targeting ligand, tumor apoptotic cell targeting ligand, tumor hypoxia targeting ligand, DNA intercalator, receptor marker, peptide, organ specific ligand, antibiotic, antifungal, glutamate pentapeptide or an agent that mimics glucose.

~~50. The reagent of claim 48, further comprising a linker between said tissue specific ligand and said ^{99m}Tc binding moiety.~~

~~51. A method of determining effectiveness of a candidate drug on a tumor, said method comprising:~~

~~a) obtaining a candidate drug;~~

~~b) conjugating said candidate drug with ethylenedicysteine (EC) to produce an EC-candidate drug conjugate;~~

~~c) chelating said candidate drug conjugate with ^{99m}Tc to produce a ^{99m}Tc-EC-candidate drug conjugate;~~

~~d) introducing said ^{99m}Tc-EC-candidate drug conjugate into a patient with a tumor; and~~

~~e) imaging said patient to determine the effectiveness of the candidate drug against the tumor.~~